The Declaration of Helsinki

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Conflict of Interest Statement

I was Director of Ethics for the World Medical Association from 2003-2006 and have been a paid consultant for the WMA since then.

Outline of Presentation

- The World Medical Association
- The Declaration of Helsinki (DoH)
- Ethics Guidelines vs. Compliance Regulations
- Ethics vs. Good Clinical Practice (GCP)
- The DoH, GCP and the FDA
- Conclusion

The World Medical Association

- Established after WW2, mainly in reaction to atrocities involving physicians
- Global representative body for physicians
- 97 National Medical Association members
- Close relationships with other international health professional associations (especially nursing, pharmacy, dentistry and physiotherapy)

WMA's Legitimacy

- No legal authority
- Sources of its moral authority
  - Pioneer in guidelines development (DoH)
  - Members' experience in health issues
  - Extensive consultation/consensus building
  - Quality of its policies and activities

Declaration of Helsinki
Brief History

- First adopted by the World Medical Association (WMA) in 1964
- Significant additions in 1975
- Minor amendments in 1983, 1989 and 1996
- Major revision and reorganization in 2000
- ‘Notes of clarification’ in 2002 and 2004
- Latest revision begun in 2007 and completed in October 2008

Declaration of Helsinki - Influence

- ICH-GCP Guidelines require adherence to "the principles that have their origin in the DoH"
- EC Directive on Clinical Trials and the U.S. FDA (until recently) require adherence to the principles of the DoH (not the current version, however)
- CIOMS Guidelines follow the DoH quite closely
- The UNESCO *Declaration on Bioethics and Human Rights* cites the DoH

Declaration of Helsinki - Influence

- DoH is by far the most cited research ethics document by research ethics committees in Africa (NEBRA, 2006; TRREE, 2009)
- Standing Committee of European Doctors (CPME) "urges EMEA and national pharmaceutical authorities to no longer accept clinical trial data that are not in accordance with the Declaration of Helsinki." (15 March 2008)

Regulations vs. Ethics Guidelines

- Regulations and laws: what **must** be done
- Ethics: what **should** be done, even if not required
- Why do more than what is required:
  - Values (altruism, compassion, justice, etc.)
  - Reputation

Principal International Ethics Guidelines

- World Health Organization (WHO): *Operational Guidelines for Ethics Committees that Review Biomedical Research* (2000, currently under review)
- CIOMS: *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (2002)
- World Medical Association, *Declaration of Helsinki* (2008)

Principal International Compliance Guidelines/Regulations

- ICH: *Guideline for Good Clinical Practice* (1996) and *Guideline: Choice of Control Group and Related Issues in Clinical Trials* (2000)
- European Commission: *Directives on Implementing Good Clinical Practice in the Conduct of Clinical Trials* (2001, 2005)
- Council of Europe: *Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research* (2004)

Ethics vs. Good Clinical Practice

- ICH (1996) defines GCP as “A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.”
- Ethics guidelines have a narrower scope and generally higher standards than GCP. They also involve consideration of how these standards should be applied in specific circumstances.

The DoH and ICH GCP – Comparison and Contrast

- Many similarities: informed consent; ethics committee approval; conduct of clinical trials
- GCP far more detailed
- Important omissions in GCP (perhaps because it is so old: E6 - 1996, E10 - 2000), e.g.
- Research on human tissues and data, including privacy/confidentiality (DoH 1, 25)
- Consideration for the environment (DoH 13)
- Access to benefits (DoH 14 and 33)

The DoH and ICH GCP – Comparison and Contrast

- Role of families and communities (DoH 18, 22)
- Clinical trials registration (DoH 19)
- Who should seek/obtain consent (DoH 24)
- Assent of incompetent research subjects (DoH 28)
- Publication of (negative) results (DoH 30)
- Enrolling patients as research subjects (DoH 31)
- Therapeutic innovation/research (DoH 35)

The DoH and the FDA

- FDA regulations on acceptance of foreign clinical studies not conducted under an investigational new drug application (IND) as support for an IND or application for marketing approval for a drug or biological product
- Until October 27, 2008 – FDA required such studies to be conducted in accordance with ethical principles stated in the Declaration of Helsinki issued by the World Medical Association, specifically the 1989 version
- Henceforth, just compliance with GCP

DoH on Placebos

Paragraph 32: “The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

- The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or

Paragraph 32 (cont.)

- Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option."

DoH on Access to Benefits

- Paragraph 14: “The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.”
- Paragraph 33: “At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.”

DoH on Human Material or Data

- Paragraph 25: “For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee.”

Conclusion

- Many different, and often conflicting, interests in research ethics
- **Interests of research subjects (individuals and communities) should prevail over those of researchers, research institutions and commercial enterprises, sponsors and funders, etc.**
- All stakeholders should aim for the highest ethical standards.

Thank You !!

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